

Application No.: 10/081,555
Filing Date: February 20, 2002
Amendment in Response to Notice to Comply (mailed 01/03/03) mailed 06/03/03
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Attorney Docket No.: SALK2270-5
(088802-5212)

Amendments to the Specification

Please replace the previous Sequence Listing with the new Sequence Listing submitted herewith.

Please insert the following acknowledgment and heading therefor after the title on page 1 of the specification as filed:

--ACKNOWLEDGMENT

This invention was made with United States Government support under Grant No. GM-26444, awarded by the National Institutes of Health. The Government has certain rights in the invention.--

Please replace paragraph [0031] with the following replacement paragraph.

-- [0031] Figure 6A presents a schematic comparison of nucleotide sequences (**SEQ ID NOs: 3-11, respectively, in order of appearance**) encoding response elements found in inducible cytochrome P450 enzymes. A database search for repeats of the sequence RGKTCA (SEQ ID NO: 41) was performed and some of the matches for enzymes involved in hepatic steroid hydroxylation are indicated. The standard nomenclature for P450 enzymes has been utilized. P450R is the single P450 oxidoreductase required for hydroxylation of steroids. UGT1A6 is a rat uridine diphosphate (UDP)-glucuronosyltransferase that conjugates glucuronic acid to hydroxylated steroids.--

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Please replace paragraph [0032] with the following replacement paragraph.

-- [0032] Figure 6B presents a schematic comparison of conserved glucocorticoid response elements found in human CYP3 genes. The region of human CYP3A4 (SEQ ID NO: 33) shown is necessary and sufficient for glucocorticoid and rifampicin induction of the full-length promoter. Corresponding regions of CYP3A5 (SEQ ID NO: 34) and CYP3A7 (SEQ ID NO: 35) are shown (Barwick et al., *Mol. Pharmacol.* 50: 10-16, 1996).--

Please replace paragraph [0039] with the following replacement paragraph.

-- [0039] Figure 8C illustrates that the DR-3 element is essential for SXR-mediated activation of CYP3A23, and is interchangeable with the IR-6 element. The wild type (DR3/WT (SEQ ID NO: 39), filled bars) or mutant forms (DR3/M1 (SEQ ID NO: 42), open bars; DR3/M2 (SEQ ID NO: 43), stippled bars; and DR3/IR6 (SEQ ID NO: 24), hatched bars) of CYP3A23 cellular promoter reporters were transfected into primary rat hepatocytes in the presence of expression vector for SXR. The ligand treatment and data presentation are the same as in 8A. RIF, rifampicin; CTZ, clotrimazole. Note the disruptions of DR-3 element (DR3/M1, and DR3/M2) abrogate the activation of CYP3A23, and the replacement of DR-3 element with IR-6 element (DR3/IR3) rescue the responsiveness.--

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Please replace paragraph [0061] with the following replacement paragraph.

--[0061] Examples of response elements suitable for use in practice of the invention methods can be selected from the following:

DR-3,4,5 = AGGTCANnAGGTCA, wherein n is 3, 4, or 5 (~~SEQ ID NOS: 44, 45, and 46 (SEQ ID NO: 44);~~

β DR-3,4,5 = AGTTCANnTGAAC, wherein n is 3, 4 or 5 (~~SEQ ID NOS: 47, 48 and 22) (SEQ ID NO: 22);~~ and

IR-6 = TGAACTNnAGGTCA, wherein n is 6 (SEQ ID NO: 23), and the like.--

Please replace paragraph [0062] with the following replacement paragraph.

--[0062] Those of skill in the art will recognize that any combination of nucleotides can be used to make up the 3, 4, 5, or 6 nucleotide spacer between the repeated half sites (i.e. N_n in ~~SEQ ID Nos: 44, 45, 46, 22, or 23~~ SEQ ID Nos: 15, 16, 17, 22, or 23).--